REMARKS

Applicants wish to thank Primary Examiner Venkat for the courteous and helpful interview conducted on August 16, 2006 with the undersigned. Applicants received a copy of the Examiner Interview Summary Record via facsimile on August 29, 2006. The Examiner confirmed during the interview that the only rejections currently pending are those under 35 U.S.C. § 112 ¶¶ 1 and 2.

Upon entry of the foregoing amendment, claims 65, 75-81, 83, 86-88, 94, 95, 99, 101, 102, and 116-118 are pending for the Examiner's consideration, with claims 65, 80, 94, 116, and 117 being the independent claims. Claims 65, 80, 94, 116, and 117 are amended herein. Applicants respectfully submit that these amendments introduce no new matter. In this regard, the Examiner is referred, for example, to page 10, lines 3-10, and pages 20-23 of the application as originally filed. Claims 1-64, 66-74, 82, 84, 85, 89-93, 96-98, 100, and 103-115 are cancelled without prejudice to or disclaimer of the subject matter contained therein.

Rejection Under 35 U.S.C. § 112 ¶ 1

Applicants have cancelled claims 103-115 directed to the aspect of the present invention that uses angle of repose to quantify flowability, without prejudice to or disclaimer of this subject matter. Accordingly, the remarks herein will focus on the pending claims, all of which are directed to the aspect of the present invention that uses flowability index to quality flowability.

The Examiner has rejected all of the claims under 35 U.S.C. § 112 ¶1, as allegedly not being enabled, citing the factors discussed in the case *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). For at least the following reasons, Applicants respectfully submit that this rejection cannot properly be maintained.

The state of the prior art and the level of predictability in the art: The Office Action repeatedly cites to an article from *Pharmaceutical Technology* entitled "On Powder Flowability" authored by Prescott and Barnum ("the Prescott article"). In particular, in an attempt to support

the position that the field is complex, unpredictable, and requires significant experimentation, the Office Action repeatedly cites to the following three passages in the Prescott article:

> ". . .no one test could ever quantify flowability." Page 60;
>
> "Flowability can never be expressed as a single value or index." Page 60; and
>
> "Currently, no universal mathematical model exists to predict powder flow behavior in every situation." Page 62.

Notably, the Office Action does not address the section of the Prescott article beginning on page 78 entitled "Flow properties as comparative, physical test methods." This section of the Prescott article makes clear that quality control checks must be performed on powders to determine if certain attributes of the powder fall within a predefined range. The Prescott article specifically notes that such quality control checks include "Carr indices," the same Carr parameters that are used to compute the flowability index recited in the claims. Pages 20-23 of the present application explain how the Carr parameters or indices are measured, and how the Carr parameters are then used to calculate a flowability index. Table 7 shows the four Carr parameters and the flowability index for four batches of conditioned microparticles, both placebo microparticles (those containing no active agent), as well as microparticles containing the active agent risperidone. As explained on page 22, the microparticles were conditioned by maintaining them at 25°C for a period of at least five days. The flowability index was found to be a good prediction of bulk material flow, and acceptable microparticle flowability occurred when the flowability index was greater than about 60.

The Prescott article explains that a flow property test, such as the Carr indices that are used to compute flowability index, could be used as a quality control test, provided that sufficient testing was done to provide the empirical limits to discern between acceptable and unacceptable batches. This is precisely what has been done in the present invention - the determination that a flowability index of 60 provides for acceptable microparticle flowability. When viewed as a whole, as it must, the Prescott article teaches one skilled in the art that Carr indices or parameters can be used as quality control or process checks for a powder once the empirical limits are established, as was done in the present invention.

The amount of direction provided by the inventors and the existence of working examples: On page 4 of the Office Action, the Examiner asserts that "applicants at page 10 admit that the micro particles are conditioned according to the process disclosed in patent 5,650,173. . ." This is incorrect. Rather, lines 3-5 on page 10 of the application read as follows: "In accordance with the present invention, a conditioning process is carried out on a finished microparticle product, such as a batch or quantity of microparticles prepared by the process disclosed in U.S. Patent Nos. 5,654,008 and 5,650,173." Thus, the process disclosed in U.S. Patent No. 5,650,173 can be used to prepare microparticles, which microparticles can then be subjected to the conditioning process of the present invention.

Applicants respectfully submit that the Examiner has not adequately considered the data provided in Table 7 on page 22 of the present application. Table 7 provides the Carr parameters, the flowability index, and the T_g (glass transition temperature) for placebo microparticles (those containing no active agent), as well as microparticles containing the active agent risperidone. These microparticles were conditioned by maintaining them at 25°C for a period of at least five days, and acceptable microparticle flowability occurred when the flowability index was greater than about 60. As shown in Table 7, the conditioning temperature of 25°C is less than the T_g (glass transition temperature) of the polymer. Thus, Applicants have provided data and examples for microparticles with and without an active agent, the conditioning process that was used, the value of the flowability index to be achieved, and how to measure the flowability index.

On page 4 of the Office Action, the Examiner appears to be discounting the articles by R.L. Carr cited on page 20 of the present application because they were published in 1965 and the Prescott article was published in 2000. Applicants respectfully submit that not only does the Examiner have to consider the entirety of the Prescott article, but also the entirety of the Carr articles, irrespective of the date they were published. A copy of each of the two Carr articles is filed herewith for the Examiner's convenience. The first Carr article is entitled "Evaluating Flow Properties of Solids." As noted on page 163 of this article, it describes "a number of standard procedures that will permit the evaluation of flow characteristics" of dry materials that

are processed in hoppers or bins. As explained on page 3, lines 16-21 of the present application, the microparticles are used with automated filling equipment where material must flow from a hopper. The Carr article goes on to explain how to measure each of the Carr parameters or indices, and how to compute the flowability index or point score, stating on page 166 that "Table II shows how these various criteria can be used in calculating a flowability point score for any type of dry material." Importantly, Table II of the first Carr article is included as Table 6 on page 21 of the present application. Finally, the Carr article explains on page 167 that "[T]his procedure gives a practical and direct way of computing a flow factor and evaluating the flowability of any material."

The Carr articles, the relevant portions of which are explained in the present application, as well as being incorporated by reference in their entirety, fully enable one skilled in the art to compute the flowability index of a particular material, and, given that information, the present invention explains how to condition microparticles to achieve a flowability index of at least 60. As shown in Table 7, one way to condition microparticles to achieve a flowability index of 60 is to maintain the microparticles at 25°C for a period of at least five days. The Prescott article explicitly recites the use of the Carr indices as one quality control check, and, therefore, is fully consistent with the method used in the claimed invention.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Table 6 on page 21 of the present application explains how to compute flowability index from the Carr indices or parameters. Table 7 presents data showing that a flowability index greater than about 60 was obtained for conditioned microparticles (maintained at 25°C for a period of at least five days), and that acceptable microparticle flowability resulted from that index. As noted on pages 21-22 of the present application, the Carr parameters and the flowability index can be measured using an automated tester, such as a Model PT-N Powder Characteristics Tester, available from Hosokawa Micron Powder Systems, Summit, New Jersey. Thus, the measurement or determination of the flowability index of a batch of microparticles is well within the ability of one skilled in the art, and no "undue" experimentation is required.

All of the independent claims recite a flowability index of about 60. Independent claims 65, 80, and 94 explicitly recite conditioning the microparticles by maintaining the microparticles at a conditioning temperature of about 25°C for a period of at least about 5 days. Independent claims 116 and 117 explicitly recite conditioning the microparticles for at least about 5 days at a conditioning temperature that is less than a glass transition temperature (T_g) of the polymer. Table 7 provides the Carr parameters, the flowability index, and the T_g (glass transition temperature) for placebo microparticles (those containing no active agent), as well as microparticles containing the active agent risperidone. These microparticles were conditioned by maintaining them at 25°C for a period of at least five days, and acceptable microparticle flowability occurred when the flowability index was greater than about 60. As shown in Table 7, the conditioning temperature of 25°C is less than the T_g (glass transition temperature). For at least all of the reasons explained above, Applicants respectfully submit that the specification fully enables one skilled in the art to practice the methods recited in the claims as presented herein. Applicants do not acquiesce to, or admit the propriety of, the enablement rejection of the claims as originally filed or previously presented.

Rejection Under 35 U.S.C. § 112 ¶ 2

The Examiner has rejected claims 68, 89, and 90 under 35 U.S.C. § 112 ¶ 2 as allegedly being indefinite. Claims 68, 89, and 90 have been cancelled herein without prejudice to or disclaimer of the subject matter contained therein, thereby rendering this rejection moot.

Conclusion

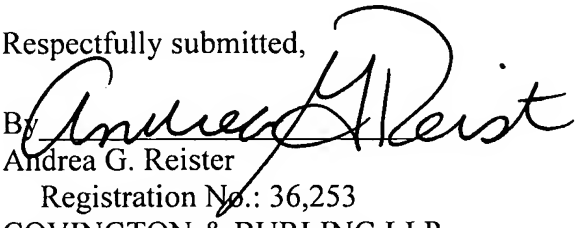
All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Dated: August 29, 2006

Respectfully submitted,

By 

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